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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,514	11/15/2001	Avi J. Ashkenazi	P2730P1C46	3254

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EXAMINER

HAMUD, FOZIA M

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 09/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/997,514

Applicant(s)

ASHKENAZI ET AL.

Examiner

Fozia M Hamud

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 119-131 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 119-131 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's preliminary amendment canceling claims 1-118 and adding new claims 119-131, filed on 15 November 2001 is acknowledged.

Thus claims 119-131 are pending and under consideration.

2. **Priority:**

2a. Based on the information given by Applicants and an inspection of the patent applications, the Examiner has concluded that the subject matter defined in this application is supported by the disclosure in application serial no. 09/941,992 filed on 28 August 2001, because, EXAMPLE 160 (Assay #111; Chondrocyte proliferation assay which demonstrates that the claimed polypeptide induces the proliferation of chondrocytes), which provides a specific and substantial asserted utility or a well established utility for the claimed polypeptides is disclosed on page 531 of Application no. 09/941,992. However, it does not appear that any of the other prior applications disclose this assay. Accordingly, the subject matter defined in claims 119-131, is afforded an effective filing date of 28 August 2001, which is the filing date of the U.S application No. 09/941,992.

Should the applicant disagree with the examiner's factual determination above, it is incumbent upon the applicant to provide the serial number and specific page number(s) of any parent application filed prior to 09/04/01, which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of and fully enabled for prior to 08/28/01.

Art Unit: 1647

Specification:

3a. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Information Disclosure Statement:

4a. References A1 and A2, cited on the PTO-1449 form submitted by Applicants on 31 May 2002 have not been considered, because they do not comply with 37 CFR 1.98(a)(2) requirements, since they fail to identify each publication by author and publication date. Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Claim rejections-35 USC § 112, first paragraph:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5a. Claims 119-124, 127-128 and 130-131 are rejected under 35 U.S.C. 112, first paragraph, while being enabling for an isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO:422, said polypeptide which induces the proliferation of chondrocytes, does not reasonably provide

Art Unit: 1647

enablement for an isolated polypeptide having at least 80%, 85%, 90%, 95% or 99% identity to the polypeptide of SEQ ID NO:422. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention.

The instant claims 119-123 are drawn to an isolated polypeptide that shares "80%, 85%, 90%, 95% or 99%" identity to the polypeptide of SEQ ID NO:422, however, the specification fails to adequately enable said polypeptides. The specification does not provide any particular conserved structure, or other distinguishing features which would enable a polypeptide having at least 80%, 85%, 90%, 95% or 99% to the polypeptide of SEQ ID NO:422, would induce the proliferation of chondrocytes. Regarding claims 124, 127-128 the specification fails to demonstrate that a polypeptide comprising only the extracellular domain of the polypeptide of SEQ ID NO:422 retains the desired activity. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity. Due to the large quantity of experimentation necessary to determine all the polypeptides comprising an amino acid sequence that is at least 80%, 85%, 90%, 95% or 99% identical to the polypeptide of SEQ ID NO:422, and to screen whether these polypeptides induce the proliferation of chondrocytes; the lack of direction/guidance presented in the specification regarding which variants of the polypeptide of SEQ ID NO:422 would retain said desired activity; the complex nature of the invention; the absence of working examples directed to variants of the polypeptide of SEQ ID NO:422; the state of the prior art establishing that biological activity cannot be predicted based on structural similarity; the

Art Unit: 1647

unpredictability of the effects of mutation on the structure and function of the claimed polypeptide and the breadth of the claims which fail to recite particular biological activities, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

5b. Claims 119-123, 124, 127, 128 and 130-131 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The instant claims 119-123 are drawn to an isolated polypeptide that shares "80%, 85%, 90%, 95% or 99%" identity to the polypeptide of SEQ ID NO:422, and claims 124, 127, 128 encompass an isolated polypeptide comprising the extracellular domain of the polypeptide of SEQ ID NO:422, however, the instant specification only describes the structure of the polypeptide of SEQ ID NO:422, and therefore, conception is not achieved until reduction to practice has occurred. Adequate written description requires more than a mere statement that it is part of the invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed

product, or any combination thereof. In the instant case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. *Vas-cath Inc. v. Mahurkar*, 19 USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." (See *Vas-cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Therefore, only the isolated polypeptide set forth in SEQ ID NO: 422, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

Art Unit: 1647

Claim rejections-35 USC § 112, second paragraph:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 119-124 and 128-131 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6a. Claims 119-124 and 128 recite ".....the extracellular domain lacking its associated signal sequence....", which renders the claims indefinite because the signal sequence is not generally considered to be part of an extracellular domain, as signal sequences are cleaved from said domains in the process of secretion from the cell. Appropriate correction is required.

Claims 129-131 are rejected under 35 U.S.C. 112, second paragraph, insofar as they depend on claim 119, 124 for the limitations set forth directly above.

Claim Rejections - 35 U.S.C. §102(b):

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7a. Claims 119-131 are rejected under U.S.C. § 102 (b) as being anticipated by Baker et al (WO9963088; published 09 December 1999).

Art Unit: 1647

Baker et al disclose an isolated polypeptide that shares 100% homology to the polypeptide of SEQ ID NO:422 of the instant application. See attached copies of the comparison of SEQ ID NO:422 of the instant invention and the sequence of the reference (SEQUENCE COMPARISON 'A'). The isolated polypeptide disclosed in the Baker et al reference lacks signal sequence. Baker et al also disclose an isolated polypeptide that comprises the extracellular domain and a chimeric polypeptide comprising said polypeptide and a heterologous polypeptide, (see claims 15, 16, 23 and 24).

Instant claims 119-131 are drawn to an isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO:422, said isolated polypeptide lacking signal sequence, an isolated polypeptide comprising the extracellular domain of the polypeptide of SEQ ID NO:422, or a chimeric polypeptide comprising said polypeptide and a heterologous polypeptide. Therefore, the Baker et al reference meets all the limitations recited in claims 119-132, anticipating said claims, in the absence of any evidence to the contrary.

7b. Claims 119-131 are rejected under U.S.C. § 102 (b) as being anticipated by Ashkenazi et al (WO200032221; published 08 June 2000).

Ashkenazi et al disclose an isolated polypeptide that shares 100% homology to the polypeptide of SEQ ID NO:422 of the instant application. See attached copies of the comparison of SEQ ID NO:422 of the instant invention and the sequence of the reference (SEQUENCE COMPARISON 'B'). The isolated polypeptide disclosed in the Ashkenazi et al reference lacks signal sequence. Ashkenazi et al also disclose an isolated polypeptide that comprises the

Art Unit: 1647

extracellular domain and a chimeric polypeptide comprising said polypeptide and a heterologous polypeptide, (see claims).

Instant claims 119-132 are drawn to an isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO:422, said isolated polypeptide lacking signal sequence, an isolated polypeptide comprising the extracellular domain of the polypeptide of SEQ ID NO:422, or a chimeric polypeptide comprising said polypeptide and a heterologous polypeptide. Therefore, the Ashenazi et al reference meets all the limitations recited in claims 119-131, anticipating said claims, in the absence of any evidence to the contrary.

7c. Claims 119-125, 130 are rejected under U.S.C. § 102 (b) as being anticipated by Walker et al (WO200029574; published 25 May 2000).

Walker et al disclose an isolated polypeptide that shares 100% homology to the polypeptide of SEQ ID NO:422 of the instant application. See attached copies of the comparison of SEQ ID NO:422 of the instant invention and the sequence of the reference (SEQUENCE COMPARISON 'C'). Walker et al also disclose a chimeric polypeptide comprising said polypeptide and a heterologous polypeptide, (see page 11, lines 16-33).

Instant claims 119-125 and 130 are drawn to an isolated polypeptide having SEQ ID NO:422 and a chimeric polypeptide comprising said polypeptide and a heterologous polypeptide. Therefore, the Walker et al reference meets all the limitations recited in claims 119-125, 130, anticipating said claims, in the absence of any evidence to the contrary.

Conclusion:

Art Unit: 1647

8. No claim is allowed.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Fozia Hamud
Patent Examiner
Art Unit 1647
23 September 2004


JANET ANDRES
PRIMARY EXAMINER